REMARKS

Formal Matters

Claims 1-9, 16 and 19 are pending after entry of the amendments set forth herein.

Claims 1-7 and 14-19 were examined and rejected.

Claims 1, 2, 4, 7, 16 and 19 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. The claims have been amended to incorporate the subject matter of dependent claims into independent claims. As such, no new matter has been added.

Claims 10-13, 14, 15, 17 and 18 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

Claim amendments

The claim amendments merely incorporate the subject matter of dependent claims 15 and 18 into independent claims 1, 2 , 4 and 7. As such the amendments set forth below raise no new issues and should be entered by the Office.

The Applicants submit that the amendments place the claims in form for allowance or in better form for appeal.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-9 and 14-19 are again rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that is assertedly inadequately described by the instant specification.

Without acquiescing to the correctness of this rejection and solely to expedite prosecution, the claims have been amended to recite a green fluorescent proteins having a sequence that is at least 95% identical to SEQ ID NO:5 or SEQ ID NO:2.

The Office Action indicates that the test for written description set forth in *Regents of the*

University of California v. Eli Lilly & Co[1], hereafter "*Lilly*" is the basis for this rejection.

The Applicants first note that *Lilly*'s tests for satisfying written description are currently in question in the U.S. Court of the Federal Circuit[2]. For example, in *Moba v. Diamond Automation*[3], judge Rader dissented to the opinion of the majority, stating that:

> In sum, the Lilly rule is not just a mere one-time mistake. It defies over thirty years of case law. It finds no specific support in any statutory language. It creates a technology-specific rule in a technology-neutral statute. It distorts the statute's rules for adequate disclosure of inventions. It complicates biotechnology patent drafting to the point of near impossibility and invites invalidating mistakes. It prices non-corporate inventors out of some biotechnological invention markets. Last, but not least, it burdens both trial and appellate courts with unnecessary and confusing procedures in otherwise simple cases like this one.[4]

Thus, Applicants respectfully submit that the tests for written description set forth in *Lilly* should not be given so much deference and weight. Doing so only repeats and amplifies the mistakes inherent in the *Lilly* tests. Instead, the tests of *Lilly* should not be regarded as "tests", but as examples of what disclosure *could* satisfy written description under §112, ¶1. In addition, the Office should consider that the examples of disclosure that would satisfy the law under *Lilly* were in the context of the case at issue in Lilly – which involved a patent application filed in 1977. Certainly the degree and detail of disclosure to satisfy the written description requirement when biotechnology was in its infancy (in 1977) must differ from that degree and detail of disclosure necessary to satisfy the written description requirement in the instant case, which was filed in the year 2000 – more than twenty five years later.

Nevertheless, Applicants respectfully submit they have met the requirements for adequate written description, even when *Lilly* is strictly applied to the present claims.

As the Office has pointed out, Lilly sets forth two test for written description:

> A description of a genus of cDNAs may be achieved by means of a recitation of **a representative number of cDNAs**, defined by nucleotide sequence, falling within the scope of the genus **or** of a recitation of **structural features** common to the members of the genus.[5]

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[1] *Regents of the University of California v. Eli Lilly & Co* 119 F.3d 1559 (Fed. Cir. 1997) at 1568-69
[2] *Moba v. Diamond Automation, Inc.*, **325 F.3d 1306** (Fed. Cir. 2003) and *Amgen Inc. v. Hoechst, Inc.*, 314 F.3d 1313, 2003 U.S. App. LEXIS 118, 65 U.S.P.Q.2D (BNA) 1385 (Fed. Cir. 2003)
[3] *Moba v. Diamond Automation, Inc.*, **325 F.3d 1306,** (Fed. Cir. 2003).
[4] Id. at 1314.

As such, according to the Lilly, the written description requirement for a genus of nucleic acids may be satisfied by a) a representative number of species, **or** b) a recitation of structural features common to all members of the species. There is no current law that requires that all species be specifically recited, even in an unpredictable art. The Applicants respectfully submit that they have satisfied both of Lilly's tests.

First, with respect to providing a representative number of species, the Applicants direct the Examiner's attention to the 41 different *Pitilosarcus* and *Renilla* GFP variants (page 8, line 4 to page 9 line 12). Applicants respectfully submit that an explicit description of 41 different examples of species encompassed by the claimed genus is representative of the claimed genus. If 41 examples of the claimed genus fails to be representative of the genus, the Applicants respectfully ask how many, in the Office's opinion, would be satisfactory?

Second, Applicants respectfully submit that the recitation of SEQ ID NOS:2 and 5 in the claims provides structural features common to all members of the claimed genus. In other words, the claimed polynucleotides encode polypeptides that share at least 95% identical to SEQ ID NO: 2 or 5, and, as such, have a shared structural feature: SEQ ID NO: 2 or 5. As such, the Applicants respectfully submit that they have met the "common structural feature" test set forth in Lilly. Further, the rejected claims allows the claimed polynucleotides to be distinguished from other polynucleotides, also satisfying further guidance set forth in Lilly.

As such, by providing the sequence SEQ ID NOS:2 and 5 and providing 41 examples of variants of each of SEQ ID NOS:2 and 5 in the specification, the Applicants respectfully submit that they have met both of the requirements for written description set forth in *Lilly*.

Finally, Applicants note that the guidance set forth in the "Synopsis of Application of Written Description Guidelines" (hereinafter "The Synopsis"), i.e., the Office's own training materials for Examination, indicates that the claims are adequately described. The Synopsis may be obtained from the following USPTO URL: http://www.uspto.gov/web/offices/pac/writtendesc.pdf.

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[5] *Regents of the University of California v. Eli Lilly & Co* 119 F.3d 1559 (Fed. Cir. 1997) at 1569.

Example 14 of the Synopsis describes a scenario that is very similar to that currently under examination. Example 14 provides an example of a specification that discloses the sequence of a polypeptide having the sequence of SEQ ID NO:3, and also discloses that the polypeptide has a certain enzymatic activity. This example also states that the specification also "contemplates but does not exemplify" variants of SEQ ID NO:3, and provides an assay for measuring the activity of the protein. In this example, the claims are directed to polypeptides having a sequence that is at least 95% identical to that of SEQ ID NO: 3 and catalyze the reaction of A→B.

The Synopsis states that the claimed subject matter is adequately described by the specification and the requirements of 35 USC §112 first paragraph have been met because "The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity.

For the Examiner's convenience, Example 14 of the Synopsis of Application of Written Description Guidelines is reproduced below:

Example 14: Product by Function

Specification: The specification exemplifies a protein isolated from liver that catalyzes the reaction of **A B.** The isolated protein was sequenced and was determined to have the sequence as set forth in SEQ ID NO: 3. The specification also contemplates but does not exemplify variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions and additions. The specification indicates that procedures for making proteins with substitutions, deletions, insertions and additions is routine in the art and provides an assay for detecting the catalytic activity of the protein.

Claim:
A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A B.

Analysis:
A review of the full content of the specification indicates that a protein having SEQ ID NO: 3 or variants having 95% identity to SEQ ID NO: 3 and having catalytic activity are essential to the operation of the claimed invention. The procedures for making variants of SEQ ID NO: 3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art.

A review of the claim indicates that variants of SEQ ID NO: 3 include but are not limited to those variants of SEQ ID NO: 3 with substitutions, deletions, insertions and additions; but all variants must possess the specified catalytic activity and must have at least 95% identity to the SEQ ID NO: 3.

Additionally, the claim is drawn to a protein which **comprises** SEQ ID NO: 3 or a variant thereof that has 95% identity to SEQ ID NO: 3. In other words, the protein claimed may be larger than SEQ ID NO: 3 or its variant with 95% identity to SEQ ID NO: 3. It should be noted that "having" is open language, equivalent to "comprising".

The claim has two different generic embodiments, the first being a protein which comprises SEQ ID NO: 3 and the second being variants of SEQ ID NO: 3. There is a single species disclosed, that species being SEQ ID NO: 3.

A search of the prior art indicates that SEQ ID NO: 3 is novel and unobvious.

There is actual reduction to practice of the single disclosed species.

The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO: 3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.

Conclusion: The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.

The Applicants respectfully submit that the fact pattern of the example set forth above is very similar to the instant fact pattern. In other words, the instant specification a) describes the sequence of a full length polypeptides (to be more exact, SEQ ID NOS: 2 and 5, and 41 variants thereof), b) describes that SEQ ID NOS: 2 and 5 have fluorescence activity, c) "contemplate but does not exemplify" variants of SEQ ID NOS: 2 and 5 (excluding the 41 variants actually exemplified), and d) provides assays for fluorescence.

As such, by the reasoning set forth in the Example 14 of the Synopsis, the instant claims should be considered adequately described by the specification, meeting the requirements of 35 USC §112, first paragraph.

In summary, the claimed subject matter meets both of the tests for written description set forth in *Lilly*, and according to the Office's own training materials, should be considered as adequately described. In view of the foregoing, the Applicants respectfully submit that the requirement for written description of 35 USC §112, first paragraph, have been met and this rejection may be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1-9 stand rejected under 35 U.S.C. § 102 (b) as being anticipated by Aran et al, assertedly because Aran discloses nucleic acids that anticipate the claims. The Applicants respectfully traverse this rejection.

The claims recite a GFP polypeptide that is at least 95% identical to SEQ ID NO:5 or SEQ ID NO:2.

Aran discloses a vector encoding an *Aequorea victoria* GFP that is less than 95% identical to SEQ ID NO:5 and SEQ ID NO:2. As such, Aran fails to disclose a GFP that is at least 95% identical to SEQ ID NO:5 or SEQ ID NO:2, as required by the instant claims and, accordingly, cannot anticipate the claimed invention.

The Applicants respectfully submit that this rejection has been adequately addressed and this rejection of claims 1-9 under 35 U.S.C. § 102 (b) may be withdrawn.

Claims 1-9 stand rejected under 35 U.S.C. § 102 (b) as being anticipated by Abedi et al, assertedly because Abedi discloses nucleic acids that anticipate the claims. The Applicants respectfully traverse this rejection.

The claims recite a GFP polypeptide that is at least 95% identical to SEQ ID NO:5 or SEQ ID NO:2.

Abedi discloses a vector encoding an *Aequorea victoria* GFP that is less than 95% identical to SEQ ID NO:5 and SEQ ID NO:2. As such, Abedi fails to disclose a GFP that is at least 95% identical to SEQ ID NO:5 or SEQ ID NO:2, as required by the instant claims and, accordingly, cannot anticipate the claimed invention.

The Applicants respectfully submit that this rejection has been adequately addressed and this rejection of claims 1-9 under 35 U.S.C. § 102 (b) may be withdrawn.

Claims 1-9 are rejected under 35 U.S.C. § 102 (e) as being anticipated by Anderson et al, assertedly because Anderson discloses nucleic acids that anticipate the claims. The Applicants respectfully traverse this rejection.

The claims recite a GFP polypeptide that is at least 95% identical to SEQ ID NO:5 or SEQ ID NO:2.

Anderson discloses a vector encoding an *Aequorea victoria* GFP that is less than 95% identical to SEQ ID NO:5 and SEQ ID NO:2. As such, Anderson fails to disclose a GFP that is at least 95% identical to SEQ ID NO:5 or SEQ ID NO:2, as required by the instant claims and, accordingly, cannot anticipate the claimed invention.

The Applicants respectfully submit that this rejection has been adequately addressed and this rejection of claims 1-9 under 35 U.S.C. § 102 (e) may be withdrawn.

Claims 4-6, 9 and 17-19 are rejected under 35 U.S.C. § 102 (e) as being anticipated by Bryan et al, assertedly because Bryan discloses a library of nucleic acids that anticipate the claims. The Applicants respectfully traverse this rejection.

The claims are directed to libraries of fusion nucleic acids that include a polynucleotide encoding a random peptide. As such, to anticipate the rejected claims, the prior art must show, *inter alia*, a polynucleotide encoding a random peptide.

At no point does Bryan disclose a nucleic acid encoding a random peptide, and, as such, Bryan cannot anticipate the claims.

The Applicants respectfully submit that this rejection has been adequately addressed and this rejection of claims 4-6, 9 and 17-19 under 35 U.S.C. § 102 (b) may be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 1-9 and 14-19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bryan (6,232,107) and Aran (Cancer Gene Ther. 4: 195-208, 1998) (Office Action page 13, item 9). . The Office Asserts that Bryan's GFP, in combination with Aran's retroviral and IRES vectors, renders the subject matter of the instant claims obvious. The Applicants respectfully traverse this rejection.

Claims 1-9 and 14-19 are further rejected under 35 U.S.C. § 103(a) as being unpatentable over Aran and Bryan (Office Action page 15, item 10).. The Office Asserts that Aran's retroviral vectors, in combination with Bryan's GFP, renders the subject matter of the instant claims obvious. The Applicants respectfully traverse this rejection.

According to MPEP §2142, an examiner must meet three basic criteria to establish a *prima facie* case of obviousness: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claim limitations.

The Applicants respectfully submit that the Office has failed to meet all three basic criteria for establishing a *prima facie* case of obvious, and, accordingly, this rejection may be withdrawn.

First, neither Bryan nor Aran disclose, teach, or otherwise suggest random polypeptides. As such, Bryan and Aran, singly or in combination, fail to teach an element of rejected claims 4, 7 and 19. Accordingly, the Office has failed to establish a *prima facie* case of obviousness for claims 4, 7 and 19 and this rejection of claims 4, 7 and 19 may be withdrawn.

Second, the Applicants respectfully submit that the Office has provided insufficient motivation, according to current law, to combine the references of Bryan and Aran to provide a *Pitilosarcus* and *Renilla* GFP in a retroviral vector. On page 14 of the Office Action, the Office states that Aran teaches favorable use of retroviral vectors, since "[T]his vector allows rapid and specific identification of the expressed protein (e.g. MDR1 gene transfer) in living cells (e.g. mammalian cells)...." On page 15 of the Office Action, the Office states that a skilled person would provide a retroviral vector with Bryan's GFP "to appreciate the benefits thereof; e.g., rapid and specific identification of the expressed protein". The Applicants respectfully submit that Aran's comments about the benefits of "[T]his vector" refer to a vector that already contains *Aequoria* GFP. In other words, Aran is merely discussing the virtues of a vector containing *Aequoria* GFP. The Applicants fail to see how this would motivate a skilled person to make a retroviral vector with a *Renilla* GFP. GFPs other than *Aequoria* GFP are not mentioned by Aran, and at no point does Aran suggest that other GFPs could be used in his vector.

As such, Aran merely provides motivation to provide a retroviral vector containing *Aequoria* GFP, not motivation to provide a retroviral vector containing a *Renilla* GFP.

In view of the foregoing, the Applicants respectfully submit that the Office has not provided adequate motivation to combine the references of Bryan and Aran. Accordingly, a *prima facie* case of obviousness has not been established and this rejection may be withdrawn

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RIGL-011.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: September 22, 2003

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